Side Effects of Praziquantel in the Treatment of Urinary Schistosomiasis in Kenya

Eisaku KIMURA[1], G.M. KAMAU[2], F.M. KILIKU[3], N.D. MUHOHO[3], P.G. WAIYAKI[3], Masaaki SIMADA[1] and Yoshiki AOKI[1]

[1]*Department of Parasitology, Institute of Tropical Medicine, Nagasaki University, 1-12-4 Sakamoto, Nagasaki 852, Japan*
[2]*Kinango Hospital, Kinango, Kwale District, Coast Province, Kenya*
[3]*Centre for Microbiology Research, Kenya Medical Research Institute, P.O. Box 54840, Nairobi, Kenya*

Abstract: Side effects of praziquantel in a single-dose treatment of urinary schistosomiasis at 40 mg/kg were studied on 174 subjects by means of questioning clinical manifestations before and 24 hr after treatment. The numbers of abdominal pain/discomfort, nausea/vomiting and dizziness/lassitude increased after treatment at a statistically significant level. "Possible" side reactions, defined as clinical manifestations developed newly or increased their degree of severity after treatment, were experienced by 55.7% of the treated people. Females suffered more nausea/vomiting than males, and people of age 16-20 years had reactions more frequently than the other ages. With a few exceptions, the adverse effects were mild and disappeared within 11 hr after their onset.

Key words: Schistosoma haematobium, Praziquantel, Side reaction, Kenya

INTRODUCTION

Praziquantel is said to be the best antischistosomal drug ever known in terms of the efficacy, safety and ease in treating patients, i. e., a single oral dose is sufficiently effective against the three common species of schistosome infecting man, *Schistosoma haematobium, S. japonicum* and *S. mansoni* (Davis *et al.,* 1979; Katz *et al.,* 1979; Santos *et at.,* 1979). The rate of parasitological cure often exceeded 90% (McMahon and Kolstrup, 1979; McMahon, 1983; Kardman *et al.,* 1983). There were no toxic effects such as teratogenicity, mutagenicity, or carcinogenicity (Frohberg and Schencking, 1981).

Side effects experienced in the treatment with praziquantel were mild and transient. The effects on laboratory biochemistry, haematology and electrocardiograms were also negligible (Davis *et al.,* 1979; Katz *et al.,* 1979; Santos *et al.,* 1979; Ishizaki *et al.,* 1979; Dias *et*

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al., 1982). However, relatively severe reactions (neuro-psychiatric, cardiovascular, hepatic, dermatological and delayed reactions) were reported in the treatment of *S. japonicum* in China (Minggang *et al.,* 1983). A report from Zaire revealed an unusually high occurrence of bloody diarrhoea among *S. mansoni* patients (Polderman *et al.,* 1984). The facts indicate a possibility that unexpected severe adverse effects might be encountered in different areas. We investigated the side effects of praziquantel in the treatment of *S. haematobium* infection, as there has been no such report in Kenya.

Materials and Methods

The present study was carried out at Mwachinga, Kwale District, Coast Province, Kenya. About 900 people were examined for eggs in the urine using a Nuclepore membrane filtration method in June/July, 1986. The egg count was expressed as the number of eggs per total volume of urine excreted in an hour (Shimada *et al.,* 1986). After a month, praziquantel was administered at a dosage of 40 mg/kg of body weight up to a maximum of 2.4 mg per one dose. Side effects produced by the treatment were studied on 224 subjects of age 13 years old and upwards. They were questioned on the existence, severity, onset and duration of clinical signs and symptoms (abdominal pain/discomfort, diarrhoea, nausea/vomiting, sense of fever, skin rash, headache, dizziness/lassitude, cough, dysuria, haematuria and others) before and 24 hr after treatment. A total of 174 paired answers (male 96, female 78) could be utilized for analyses, of which egg counts were available for 74 persons.

For statistical analysis, chi-square test was employed.

Results and Discussion

The occurrence of clinical manifestations was compared before and 24 hr after treatment (Table 1). Abdominal pain/discomfort, nausea/vomiting and dizziness/lassitude increased in number after treatment at a statistically significant level ($p<0.01$), suggesting that the manifestations were side reactions caused by the treatment. The numbers of sense of fever, cough, dysuria and haematuria decreased significantly ($p<0.01$). If the decreases resulted from immediate effects of praziquantel was not certain from the present study. No Differences were seen in diarrhoea, skin rash and headache.

The occurrence of "possible" side reactions, which were defined as clinical manifestations developed newly or increased their degree of severity after treatment, was analyzed by sex (Table 2). Of 174 patients of both sexes, 97 (55.7%) had the reaction (s), among which dizziness/lassitude was the commonest (27.6%), followed by nausea/vomiting (25.9%) and abdominal pain/discomfort (23.6%). Females had significantly more nausea/vomiting than males ($p<0.05$). The reason was not known. Headache was observed in relatively high percentages of the treated males (16.7%) and females (12.8%). Several previous studies also reported headache after treatment (Davis *et al.,* 1979; Katz *et al.,* 1979; Kardman *et al.,* 1983). Skin rash, fever and diarrhoea were rare.

The occurrence of "possible" reactions was further analyzed by age (Table 3) and pre-treatment egg count (Table 4). The age group 16-20 years had reactions more frequently ($p < 0.05$), and the age group 36 years and upwards had them less frequently ($p < 0.05$) compared with the other age groups. Also, nausea/vomiting was found to be more common under 21 years old ($p < 0.05$). The tendency of having more side reactions under 21 years than in

Table 1. The number of clinical manifestations reported before and 24 hr after treatment with praziquantel

	Pre-treatment	Post-treatment
Abdominal pain/discomfort	19 (10.9)	42 (24.1) *
Diarrhoea	6 (3.4)	6 (3.4)
Nausea/vomiting	5 (2.9)	48 (27.6) *
Sense of fever	20 (11.5)	3 (1.7) **
Skin rash	9 (5.2)	5 (2.9)
Headache	70 (40.2)	65 (37.4)
Dizziness/lassitude	50 (28.7)	77 (44.3) *
Cough	28 (16.1)	11 (6.3) **
Dysuria	71 (40.8)	30 (17.2) **
Haematuria	87 (50.0)	44 (25.3) **
No. person studied	174 (100)	174 (100)

( ): Percentage of the total number of persons studied.
*: Increase significant at 1% level.
**: Decrease significant at 1% level.

Table 2. The occurrence of "possible" side reactions analyzed by sex

	Male	Female	Total
Abdominal pain/discomfort	24 (25.0)	17 (21.8)	41 (23.6)
Diarrhoea	2 (2.1)	3 (3.8)	5 (2.9)
Nausea/vomiting	19 (19.8)	26 (33.3)	45 (25.9)
Sense of fever	0 (0.0)	1 (1.3)	1 (0.6)
Skin rash	1 (1.0)	1 (1.3)	2 (1.1)
Headache	16 (16.7)	10 (12.8)	26 (14.9)
Dizziness/lassitude	27 (28.1)	21 (26.9)	48 (27.6)
No. person with rection(s)	53 (55.2)	44 (56.4)	97 (55.7)
No. person without reaction	43 (44.8)	34 (43.6)	77 (44.3)
No. person studied	96 (100)	78 (100)	174 (100)

( ) : Percentage of the total number of persons studied.

Table 3. The occurrence of "possible" side reactions analysed by age group

	Age group				Total
	13−15	16−20	21−35	36−	
Abdominal pain/discomfort	17 (27.4)	10 (31.3)	10 (22.7)	4 (11.1)	41 (23.6)
Nausea/vomiting	22 (35.5)	10 (31.3)	8 (18.2)	5 (13.9)	45 (25.9)
Headache	6 (9.7)	5 (15.6)	9 (20.5)	6 (16.7)	26 (14.9)
Dizziness/lassitude	18 (29.0)	12 (37.5)	12 (27.3)	6 (16.7)	48 (27.6)
No. person with reaction(s)	36 (58.1)	23 (71.9)	24 (54.5)	14 (38.9)	97 (55.7)
No. person without reaction	26 (41.9)	9 (28.1)	20 (45.5)	22 (61.1)	77 (44.3)
No. person studied	62 (100)	32 (100)	44 (100)	36 (100)	174 (100)

( ) : Percentage of the total number of persons studied.

Table 4. The occurrence of "possible" side reactions analysed by egg count

	Pre-treatment egg count/hr				Total
	−10	11−100	101−500	501−	
Abdominal pain/discomfort	3 (14.3)	6 (27.3)	1 (6.7)	2 (12.5)	12 (16.2)
Nausea/vomiting	5 (23.8)	8 (36.4)	5 (33.3)	4 (25.0)	22 (29.7)
Headache	3 (14.3)	4 (18.2)	3 (20.0)	3 (18.8)	13 (17.6)
Dizziness/lassitude	8 (38.1)	4 (18.2)	4 (26.7)	2 (12.5)	18 (24.3)
No. person with reaction(s)	10 (47.6)	17 (77.3)	7 (46.7)	7 (43.8)	41 (55.4)
No. person without reaction	11 (52.4)	5 (22.7)	8 (53.3)	9 (56.3)	33 (44.6)
No. person studied	21 (100)	22 (100)	15 (100)	16 (100)	74 (100)

( ) : Percentage of the total number of persons.

Table 5. The onset (min. after drug administration) and duration of "possible" side reactions

		Onset (min)		Duration(min)	
	No. person	Average	Range	Average	Range
Abdominal pain/discomfort	39*	98.9	1−360	207.4	20−660
Nausea	37	126.6	1−480	149.9	10−420
Vomiting	5	188.0	60−360	vomited 1−2 times	
Headache	18**	244.5	1−600	198.3	30−600
Dizziness/lassitude	47***	145.0	1−540	161.2	10−600

*: In another three persons, the pain persisted for more than 23 hr.
**: In another five persons, the headache persisted for more than 15 hr.
***: In another person, the symptom persisted for more than 23 hr.

the older ages could not be attributed to a higher average egg count among young patients, because no association was found between the level of pre-treatment egg count and the frequency of reactions ($p<0.10$). Similar observation was made in Tanzania by McMahon and Kolstrup (1979).

The onset of reactions (min after drug administration) and their duration (min) were set out in Table 5. Most of the reactions disappeared without particular treatment within 11 hr after their appearance. Out of 155 cases with data on the duration, 9 (5.8%) experienced reactions (headache, abdominal pain or dizziness) which persisted for more than 15 hr. In the treatment of *S. japonicum* in China, long-lasting adverse effects, which incapacitated 0.11% of the treated patients for up to more than 12 months, were reported (Minggang *et al.*, 1983).

In the present study, the side effects recorded were mostly mild. Only two persons (1.1% of the treated) complained severe reactions, i. e., abdominal pain and headache in one person, and headache in the other.

The side effects of praziquantel in the treatment of urinary schistosomiasis were found to be very common but mild and short-lasting, which disappeared without particular treatment. The drug could be administered with more confidence of safety in the future control of schistosomiasis in this area.

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